#35
Amend B

1Patent
Attorney's Docket No. 001560-377

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of	)	
	)	
Keiko SAKAKIBARA et al.	)	Group Art Unit: 1655
	)	
Application No.: 09/446,089	)	Examiner: Juliet C. Einsmann
	)	
Filed: December 17, 1999	)	Confirmation No.: 1763
	)	
For: GENE ENCODING A PROTEIN HAVING AURONE SYNTHESIS ACTIVITY	)	

REPLY AND AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In complete response to the Official Action dated February 27, 2002, please amend the above-identified application as follows:

IN THE CLAIMS:

Please cancel claims 10-17 without prejudice or disclaimer.

Please replace claims 1, 2, 4 and 5 as follows:

B1

1. (Amended) An isolated gene encoding a protein having activity to synthesize aurones by preferentially using chalcones as substrates.

B1 cont.

2. (Amended) An isolated gene obtained from a plant, which encodes a protein having activity to synthesize aurones by preferentially using chalcones as substrates.

B2

4. (Twice Amended) An isolated gene as set forth in claim 1, which hybridizes under high stringency conditions with a nucleic acid having the nucleotide sequence described in SEQUENCE ID NO:1, and encodes a protein having activity to synthesize aurones by preferentially using chalcones as substrates.

5. (Twice Amended) An isolated gene as set forth in claim 1, which encodes an amino acid sequence having a homology of at least 55% relative to the amino acid sequence described in SEQ ID NO:2, and encodes a protein having activity to synthesize aurones by preferentially using chalcones as substrates.

7. (Amended) A host cell transformed by a vector as set forth in claim 6.

B3

8. (Amended) A host cell as set forth in claim 7, wherein said host cell is a microorganism or animal cell.

9. (Amended) A host cell as set forth in claim 7, wherein said host cell is a plant cell.

Please add new claims 18-26 as follows:

--18. (New) An isolated nucleic acid encoding a protein having activity to synthesize aurones by preferentially using chalcones as substrates.

B4

19. (New) An isolated nucleic acid obtained from a plant, which encodes a protein having activity to synthesize aurones by preferentially using chalcones as substrates.

20. (New) An isolated nucleic acid as set forth in claim 18, encoding a protein having the amino acid sequence described in SEQ ID NO. 2 or an amin oacid sequence modified by deletion, substitution and/or addition of one or more amino acids relative to that amino acid sequence, and havnig actiity to sythesize aurones by preferentialy using chalcones as substrates.

21. (New) An isolated nucleic acid as set forth in claim 18, which hybridizes under high stringency conditions with a nucleic acid having the nucleotide sequence described in SEQUENCE ID NO:1, and encodes a protein having activity to synthesize aurones by preferentially using chalcones as substrates.

22. (New) An isolated nucleic acid as set forth in claim 18, which encodes an amino acid sequence having a homology of at least 55% relative to the amino acid sequence

described in SEQ ID NO:2, and encodes a protein having activity to synthesize aurones by preferentially using chalcones as substrates.

23. (New) A vector comprising a nucleic acid as set forth in claim 18.

By Cont.

24. (New) A host cell transformed by a vector as set forth in claim 23.

25. (New) A host cell as set forth in claim 24, wherein said host cell is a microorganism or animal cell.

26. (New) A host cell as set forth in claim 24, wherein said host cell is a plant cell.--

REMARKS

Entry of the foregoing, reexamination and reconsideration of the above-identified application are respectfully requested.

Claims 1-9 have been rejected under 35 U.S.C. §112, first paragraph, as allegedly not being enabled by the specification. This rejection is respectfully traversed.

The Official Action acknowledges that the specification enables a nucleic acid encoding a protein having activity to synthesize aureusidin by using chalcones as substrates, wherein the nucleic acid comprises a sequence encoding SEQ ID NO: 2. However, the specification allegedly does not enable other nucleic acids encoding such proteins or other nucleic acids encoding proteins having the ability to synthesize any other aurones, or for the gene encoding SEQ ID NO:2. The specification is said to teach a single cDNA molecule (SEQ ID NO:1) which encodes the polypeptide of SEQ ID NO:2. The polypeptide encoded by SEQ ID NO:1 has the ability to synthesize aureusidin by using chalcones as substrates. The specification is further said to teach that the enzyme tyrosinase from the organisms Neurospora also has the ability to synthesize aureusidin by using chalcones as substrates. The nucleic acid encoding the Nuerospora tyrosinase was allegedly known in the prior art at the time of the invention. According to the Examiner, the specification is silent to other polypeptide that can synthesize aureusidin by using chalcones as substrates, or any polypeptide that have the ability to synthesize any other aurones (other than aureusidin) from chalcones. While there are said to be many polyphenol oxidase molecules known in the art, there is allegedly no guidance that would

lead one skilled in the art to select the nucleic acids which encode polypeptide having the ability to synthesize aureusidin by using chalcones as substrates, or the ability to synthesize any other aurone using chalcones as substrates. The Examiner further notes that the claims recite "genes" which encode the proteins; however, no full length "gene" sequence encoding SEQ ID NO:2 is allegedly provided. With respect to the language in the claims that the sequence can be modified, the specification allegedly fails to provide guidance as to which and how many amino acids can be modified. Identifying other nucleic acids falling within the scope of the claims would allegedly require screening of all possible enzymes to see if they have the recited functionality.

Each of these assertions is respectfully believed to be in error. The Official Action mentions on page 6 about "the large quantity of experimentation necessary to identify other members of the claimed group." This, however, is not the proper standard. Instead, it is the *quality* of the experimentation that must be measured to determine whether it is undue. If the experimentation is merely routine, then no undue experimentation would be required even if it would take time. Moreover, the specification does not have to teach how to identify all members of the claimed group. Instead, one skilled in the art would have to be enabled to make and use the claimed genes.

It is respectfully submitted that one skilled in the art would be able to practice the invention as claimed based upon the teachings of the specification in light of the knowledge in the art. Using the sequence of SEQ ID NO:1 as a probe, one skilled in the art could readily obtain other sequences which could encode a protein having activity to synthesize

aurones as instantly claimed. This is described in the specification at, for example, page 7, line 37 - page 8, line 11.

With respect to the recitation of "gene" in the claims, it is noted that the claims have been amended to recite that the gene is "isolated." The specification specifically staes that "gene for this aurone synthase, which syntesizes aurones by using chalcones as substrates, was obtained from a cDNA library prepared from the petal of snapdragon, based on the partial amino acid sequences as described above." Page 3, lines 4-8. A "gene" is thus described in the specification and one skilled in the art would be enabled to obtain the full length gene using the sequences identified in the specification. Genes of the invention are also described as being obtainable by hybridization with nucleic acid having the nucleotide sequence of SEQ ID NO:1 under stringent conditions. Page 6, lines 17-34. The specification further states that "to obtain a genomic DNA, a genomic DNA library is prepared from snapdragon in accordance with a conventional method, and this is then screened in accordance with a conventional method by cDNA or its fragment." Page 7, lines 20-28. The specification further states at from page 7, line 37 - page 8, line 11:

> Naturally-occurring genes, that hybridize with nucleic acid having the nucleotide sequence described in SEQ ID NO. 1 and that encodes an enzyme having activity to synthesize aurones by using chalcones as substrates, are obtained by preparing a cDNA library or genomic DNA library from a plant which has ability to produce a protein having aurone synthase activity in accordance with a conventional method, and then screening the library by using, for example, cDNA or its fragment having the nucleotide sequence shown in SEQ ID NO. 1 as a probe. The above-mentioned conditions can be used for the hybridization at this time.

Based upon the above, it is respectfully submitted that the specification enables one skilled in the art to obtain the instantly claimed genes.

New claims 18-26 are also enabled by the specification. These claims recite the isolated "nucleic acid" encoding a protein, rather than the isolated "gene." No new matter is added by this amendment. The disclosed sequences are clearly "nucleic acid" sequences.

In view of the above, withdrawal of the rejection of record is respectfully requested. Such action is believed to be in order.

Claims 1-9 have also been rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter not described by the specification. This rejection is respectfully traversed.

The Official Action notes that the claimed genus is large but only one species is described. Claims 1-3 are asserted to not provide "structure" to define the claimed nucleic acid. It is respectfully submitted that the instant specification would describe the claimed genus to a person skilled in the art. As stated *supra*, the application describes how one skilled in the art could readily obtain additional genes and nucleotide sequences which encode the claimed genes.

With respect to claim 4, it is asserted that there is no requirement regarding the stringency of hybridization. Claim 4 has been amended to recite that the hybrization occurs under "high" stringency conditions. We note that the stringency is defined at page 6 of the application as being 5 x SSC at 50°C, preferably 2 x SSC at 50°C, and more preferably 0.2 x SSC at 50°C.

In view of the above, withdrawal of this rejection of record is respectfully requested and believed to be in order.

Claims 4, 5 and 7 have been rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. This rejection is respectfully traversed.

In claim 4, "capable of hybridizing" and "under stringent conditions" are allegedly unclear. The "capable of hybridizing" has been amended to recite "which hybridizes," as helpfully suggested by the Examiner In claim 4, the recitation of under stringent conditions has been amended to recite that the conditions are "high" stringency conditions.

For claim 5, it is noted that the gene is a nucleic acid and questions how a nucleic acid can have sequence homology to an amino acid. This claim has been amended to recite that the gene encodes an amino acid sequence which is homologous to the SEQ ID NO:2 amino acid sequence.

For claim 7, the meaning of "host" is allegedly unclear. As helpfully suggested by the Examiner, the claim has been amended to recite a "host cell." Therefore, transgenic animals are no longer encompassed by the claim.

In view of the above, withdrawal of this rejection of record is respectfully requested and believed to be in order.

Claims 1-5 have been rejected under 35 U.S.C. §101 as the claims are allegedly directed to non-statutory subject matter. The claims allegedly do not indicate the claimed subject matter is isolated from its natural form. This rejection is rendered moot by the

instant amendment. The claims have been amended, as helpfully suggested by the Examiner, to recite that the claimed genes/nucleic acids are isolated.

Withdrawal of this rejection is thus respectfully requested. Such action is believed to be in order.

Claims 1-8 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Kupper et al (*Journal of Biological Chemistry*, 264(29):17250-58 (1989). This rejection is respectfully traversed.

The Federal Circuit has previously held that prior art is anticipatory only if every element of the claimed invention is disclosed in a single item of prior art in the form literally defined in the claim. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 90 (Fed. Cir. 1986), *cert denied*, 480 US 947 (1987). This standard is clearly not met in the instant application.

Kupper et al teaches the gene encoding tyrosinase from Neurospora. Tyrosinase is said to have been shown in Example 18 of the specification to be able to synthesize aurones by using chalcones. However, unlike applicants' claimed gene, the tyrosinases of Neurospora origin have very broad substrate specificity. The enzymes of applicants' claimed invention do not have tyrosinase activity (*see, e.g., FEBS Letters*, 499(2001): 107-111, copy enclosed herewith). Since the enzyme of the present invention preferentially uses chalcones as substrates, the claimed invention is distinguishable over the Tyrosinases of the prior art. Each recitation of the claims is not met by the cited art.

In view of the above, withdrawal of the rejection of record is respectfully requested. Such action is believed to be in order.

Claims 1-9 have been rejected under 35 U.S.C. §102(e) as allegedly being anticipated by Robinson (U.S. Patent No. 6,242,221). This rejection is respectfully traversed.

The nucleic acid taught by Robinson is said to encode a polypeptide having 64% identity with SEQ ID NO: 2. This nucleic acid is said to be capable of hybridizing to SEQ ID NO: 1 of the instant invention under some stringency conditions. This aspect of the rejection is now moot in view of the amendment to the claim 4, for example, which states that the gene hybridizes under high stringency. While Robinson does not teach that the polyphenol oxidase disclosed has the activity to synthesize aurones from chalcones, the specification is quoted as stating that "enzymes having polyphenol oxidase activity clearly have activity to synthesize aurones by using chalcones as substrates" (p. 8). These enzymes, however, would not "preferentially" synthesize aurones as now required by the claims.

Withdrawal of this rejection is respectfully requested and believed to be in order.

Claims 1-7 and 9 have also been rejected under 35 U.S.C. §102(b) as allegedly being anticipated by McBride et al (WO 96/40951). This rejection is respectfully traversed.

McBride et al is said to teach a nucleic acid encoding a protein having activity to synthesize aurones by using chalcones as substrates. McBride is said to teach vectors

comprising genes encoding tyrosinases and ORF438 from Streptomyces antibioticus. The encoded polypeptide is asserted to read on, for example, claim 3 by the language regarding modifications of the sequence, and claim 4 since the degree of stringency is not defined. For claim 5, the functional limitation is asserted to be met. These assertions are in error.

The cited reference does not disclose or even suggest a gene or nucleic acid encoding a protein which will synthesize aurones preferentially using chalcones as substrates, as recited in each of the claims. With respect to claim 4, the claim now requires hybridiation under "high" stringency conditions. The reference thus fails to anticipate the claimed invention.

Withdrawal of the rejection of record is respectfully requested. Such action is believed to be in order.

Further and favorable action in the form of a Notice of Allowance is respectfully requested.

In the event that there are any questions relating to this amendment or the application in general, it would be appreciated if the Examiner would contact the undersigned attorney by telephone at 508-339-3684 so that prosecution would be expedited.

Respectfully submitted,

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